UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,859	09/26/2003	Michael E. O'Donnell	22221/1120 (RU 339)	8720

7590 06/01/2006

Nixon Peabody LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603-1051

EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,859	O'DONNELL ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-13* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I,claims 1-13, to the delta subunit, in the paper of 5/3/2006, is acknowledged. The traversal is on the ground(s) that the basis asserted by the PTO to justify restriction does not support restriction in this application because the standard to determine whether inventions are unrelated (and restriction may be justified) requires a showing that the inventions "are not disclosed as capable of use together, having different modes of operation, different functions and different effects" and that the PTO merely asserts that the delta, delta prime and tau polypeptides have different functions and effects. Applicants submit that assertion, even if true, fails to meet the standard for restriction because the three subunits are capable of use together. Applciants submit that because the inventions are capable of use together, the inventions are related and thus restriction is improper.

Applciants complete traversal is acknowledged, however, is found nonpersuasive on the basis that even if the inventions are related, the related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and "the inventions as claimed are either not capable of use together **or** can have a materially different design, mode of operation, function, or effect". See MPEP § 806.05(j). In the instant case, while the inventions are capable of use together, they "have a materially different design, mode of operation, function and effect".

While it is acknowledged that the inventions are capable of use together, the claims are examined to the extent that theyare drawn to the elected group I, the delta subunit, even though the claim may require subunits, in addition to the delta subunit.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure statement filed on 9/26/2003, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

Applicants claim that the instant application is a continuation of Application Serial Number: 09/716,964, is objected to on the basis that the recitation in claims 1 and 6, "comprising at most about 0.9M sodium citrate buffer at a temperature of at least about 37°C" is not supported by the specification of Application Serial Number 09/716,964 and thus relative to the parent application would be considered new matter.

Appropriate correction is required.

Claim Objections

Claims 1 and 6 are objected to because of the following informalities:

Claims 1 and 6 each recite "hybridizes to the complement of SEQ ID NO: 177...".

For the sake of clarity it is suggested that these be amended to recite "hybridizes to the **complete** complement of SEQ ID NO: 177..."

Claim 3 depends from rejected claim 1.

Claims 1-13 are objected to because each of the claims contains non-elected to subject matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite in that it is drawn to the isolated Bacillus subunit according to claim 1, wherein the subunit is purified. It is unclear how claim 7 further limits claim 1 from which it depends, because it is unclear how an "isolated subunit" is not also a "purified subunit". Because applicants intended difference in the meaning of "isolated" and "purified" is unclear and confusing, claim 7 is indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13 are directed to all possible isolated *Bacillus* species delta subunits of a DNA polymerase III-type enzyme, encoded by a nucleic acid molecule which hybridizes to the complement of SEQ ID NO: 177, under conditions comprising at most about 0.9M sodium citrate buffer at a temperature of at least 37°C. The specification, however, only provides a single representative species isolated from *Bacillus stearothermophilus* comprising the complete amino acid sequence of SEQ ID NO: 178 encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these enzymes by any identifying structural characteristics or properties other than those listed in claim 1, for which no predictability of function is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. In the instant specification, a delta subunit protein of a DNA polymerase III-type enzyme is fully described in the form of SEQ ID NO: 178.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 2, 4-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *Bacillus* delta subunit of a DNA polymerase III-type enzyme, comprising **the** amino acid sequence of SEQ ID NO: 178, does not reasonably provide enablement for any delta subunit of a DNA polymerase III-type enzyme from any *Bacillus* species, encoded by a nucleic acid molecule hybridizing to the complement of SEQ ID NO: 177 under conditions comprising at most about 0.9M sodium citrate buffer at a temperature of at least about 37°C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 2, 4-13 are so broad as to encompass any delta subunit of a DNA polymerase III-type enzyme from any *Bacillus* species, encoded by a nucleic acid molecule hybridizing to the complement of SEQ ID NO: 177 under conditions comprising at most about 0.9M sodium citrate buffer at a temperature of at least about 37°C. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place minimal structural limits on the claimed polypeptides and no functional limits on the claimed polypeptides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that *Bacillus* delta subunit of a DNA polymerase III-type enzyme, comprising **the** amino acid sequence of SEQ ID NO: 178.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any delta subunit of a DNA polymerase III-type enzyme from any *Bacillus* species, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity; (B) the general tolerance of delta subunit to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue and of a delta subunit with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: 65, IDS submitted on 9/25/2003), it would require undue experimentation for one skilled in the art to arrive at the majority of those subunit polypeptides of the claimed genus having the desired activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims broadly including any delta subunit protein from any *Bacillus* species which is encoded by a nucleic acid molecule which hybridizes to the complement of SEQ ID NO: 177 under conditions comprising at most about 0.9M sodium citrate buffer at a temperature of at least about 37°C. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those subunit polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
5/24/2006